

HEMATOLOGICAL STUDIES IN TUBERCULOSIS.¹

BY ARNOLD C. KLEBS, M.D.,

CONSULTING PHYSICIAN TO THE COOK COUNTY HOSPITAL FOR CONSUMPTIVES, DUNNING,
ILLINOIS,

AND

HENRY KLEBS, M.D.,

OF CHICAGO.

NOT very long ago the opinion prevailed that in tuberculosis, particularly its pulmonary form, examination of the blood could not reveal any marked changes, such as one would expect from the apparent anemia and the more or less marked lesions in the lungs. This refers more particularly to the condition and number of the erythrocytes and to the hemoglobin, the leukocytes receiving only scant attention and the reports of alterations in their number being confusing and contradictory. A very good historical review of this subject has recently been given by Ullom and Craig,² so that it is not necessary for us to enter into it again. In this article the authors give also the results of their own investigations, embracing thirty-nine cases, together with a *resume* of the modern work done on this subject up to the middle of 1905.

Since this time two new investigations have been reported—by Arneth³ and Kjer-Peterson.⁴ On account of the great numbers of observations made, the methods used, and the perfection and refinement of technique not heretofore employed, these two studies command close attention. They both attempt to bring order into the confusion which has characterized thus far our conceptions in regard to the leukocytic elements in the blood of tuberculous individuals. Everything in this direction is eminently welcome, at a time when we are becoming more and more convinced of the fundamental role of the leukocytes in natural and acquired immunity. During the last winter, with the assistance of Dr. Milton W. Hall, we began a series of systematic investigations,⁵ based upon the methods given in these investigations, particularly that of Arneth's.

If we give here a preliminary report of the results without being able to draw definite and exact conclusions, we do so because we

¹ Read at the meeting of the National Association for the Study and Prevention of Tuberculosis, Washington, D. C., May 17 and 18, 1906.

² Examination of the Blood in Pulmonary Tuberculosis, with Special Reference to Prognosis. AMERICAN JOURNAL OF THE MEDICAL SCIENCES, September, 1905.

³ Die Lungenschwindsucht auf Grundlage klinisches und experimenteller haematologischer Untersuchungen, Johann Ambrosius Barth, Leipzig, 1905.

⁴ Ueber die numerischen Verhältnisse der Leukocyten bei der Lungentuberculose, Würzburg, 1906.

⁵ The investigations were made at the Cook County Hospital for Tuberculosis at Dunning, Illinois, and at the Chicago Laboratory. At the former, Dr. E. S. Moore, resident physician at the hospital, gave much valuable assistance in the work.

feel that in a complex subject like this, involving many laborious examinations, any contribution may prove helpful in future investigations. A more detailed report on this subject will be made in the near future.

Before reporting on our own results we shall give a brief review of the investigations mentioned. Kjer-Peterson, in the first part of his work, dealing with the normal numerical relations of leukocytes in the blood, after a careful analysis of the literature on the subject, comes to the conclusion, that our present-day conception of the subject is based on the results of uncritical and unscientific examinations. His technique for the leukocyte count does not differ essentially from that employed before. He uses the ordinary Thoma-Zeiss chamber without divisions, counting the whole visual field as a unit, according to Thoma's method (quotients to be calculated for each microscope, as has been done for some time in this country), but an enlargement of seventy only, instead of Thoma's two hundred, and always with ocular divisions. For diluting fluid he uses 0.3 per cent. acetic acid solution with methyl violet, and he counts in dilutions of 1 to 20. By this method he is able to count much more rapidly than with any other, and by an exact determination of sources of error, to which he has given particular and painstaking attention, he believes that he can always obtain accurate and uniform results. The average error in his examinations does not exceed 8 per cent., which corresponds to a great degree of accuracy. He does not consider any work exact in which the percentage of error is not determined.

If the above method, for details of which we have to refer to the original, is carried out with the precaution referred to, repeated counts become unnecessary, except for the determination of the "homogeneity" of the blood. Drops of blood taken successively from blood coming from the same puncture do not always contain the same number of leukocytes per unit volume. Kjer-Peterson calls such blood "inhomogeneous," and the counting of leukocytes in such cases does not give figures which can be used as the expression for the actual number of leukocytes. "Homogeneity," therefore, must be determined before the counting can become of practical value.

With this additional precaution, Kjer-Peterson has made numerous counts in healthy individuals. He comes to results which among themselves are quite uniform, but much at variance with those obtained by other observers. This part of his work is of particular interest, since we cannot but be conscious of the uncertainty of our knowledge in this respect, each observer apparently having his own normal standard and using the term "leukocytosis" in conformity therewith.

The number of leukocytes in the blood of healthy adults per c.mm. as usually given ranges between the widely separated limits

of 5000 and 10,000, with some variation as to the upper and lower limits. (Grawitz, Engel, Halla, Rieder, v. Jaksch, etc.) The French observers, however, seem to have adopted a narrower and lower "normal" zone (Hayem, Malassez, Grancher, Bouchut and Dubrisay, etc.). Arneth seems to be the only German observer who restricts the normal range to 5000 and 6000, and in this restriction goes even farther than the French school. Kjer-Peterson is at variance with all other observers, in that he maintains that it is impossible to give a definite level for the normal leukocytic curve of men and women, since they differ essentially. He finds for healthy men a nearly uniform and constant level of the curve between 4000 and 5000, with individual differences rarely going above 5000 and never below 3500. In healthy women, on the other hand, he finds all figures between 3000 and 24,000. He obtained these figures from examinations made early in the morning, upon the patient's awakening, and before the first meal. He insists on this time as the best for obtaining uniform and comparable results, although he doubts that digestion has any influence at all on the leukocytic curve, while motion and exertion seem to affect the curve decidedly, though only temporarily. Another difference noted between the leukocytic curve of men and women is that the curve of the former shows a straight and constant level, while the course in the latter is given to great variations, the blood, therefore, showing "inhomogeneity." He comes to his conclusion from his examinations of five men and thirteen women, a small material, as he himself admits, especially in the case of the men, but he believes this objection to have been overcome by continuing the study of each individual for long periods.

In regard to the subject which particularly interests us, that of pulmonary tuberculosis, his results are based on a carefully analyzed material of 142 men and 171 women, mostly patients of the Vejle-fjord Sanatorium. This certainly must command attention, particularly when we consider the painstaking attention which was given to every detail of technique and the series of single examinations. The author classifies his cases according to the intensity and extent of the pathological process in each, and since we have based our own classification upon his, we shall outline his method here.

Like the one adopted by the National Association for the Study and Prevention of Tuberculosis this classification is based on the one of Turban. The Roman numerals indicate various degrees of the anatomical extension of the process. To these Kjer-Paterson adds further symbols, indicating thereby other characteristics, particularly in regard to the intensity of the process. This has been attempted similarly by Turban and Meissen, but Kjer-Peterson's symbols seem to me to give more clearly a condensed description of a case in regard to its intensity and extent.

Each stage¹ is divided into active (*A*) and passive (*P*) cases. He calls active cases those with general constitutional symptoms, which indicate progress of the disease, fever (normal is 98° to 99.7° F. maximum rectal), night sweats, emaciation, or local symptoms, as hemoptysis, and also cases in which the history and examination reveal that the local process is more or less in a state of development. Passive cases are those in which the above symptoms are not found.

The defects of any such classification in its practical application are, of course, also inherent in this one, especially as the determination of activity or passivity gives great latitude to individual difference of opinion. Kjer-Peterson satisfied the claim for great objectivity, however, by having each case independently classified by a clinical authority and by giving very exact case histories.

With this general subdivision of his material he gives the results of his examinations and tries to establish the possible causal relations between the numerical relations in his cases and the various incidents in the course of the disease. He takes exception to the work of Appelbaum, which is always regarded as authoritative, and calls it "a collection of theories and postulates, without there being presented a single figure to substantiate the theses." On the other hand, the results of his examinations of the whole coincide more with those of Stein and Erbmann,² who came to the following conclusions:

1. Increase of leukocytes in tuberculous individuals, if there is not present a chronic, prevalent or exudative, inflammatory process, speaks for cavity formation in the lung.³

2. The beginning of cavity formation in a case can be determined by consecutive counts of the leukocytes, and by a sudden increase in their number after a prolonged normal period.

3. Cavity formation can be excluded in most cases, if normal numerical conditions are found. The increase of the leukocytes is not due to the tuberculous virus as such, but is a consequence of septicemia, caused by certain highly virulent bacteria, not by

¹ The upper two right lobes or two half lobes are always counted as one.

I. Stage. I A (Active).

I P (Passive).

II. Stage. II A (Active).

II P (Passive).

III. Stage. III A Disease stationary or retrogressive.

III A_{1a} Afebrile case.

III B_{1b} Occasional temperatures of 100° to 101.3° F. (rectal).

III A_{1c} One or more periods of temperature above 101° F.

III A₂ Advancing though intermittent cases.

III A₃ Continuously advancing cases.

III P₁ Passive cases with predominating sclerotic processes (stethoscopic finding).

III P₂ Passive cases with predominating destructive processes (stethoscopic finding).

² Zur Frage der Leukocytose bei tuberculösen Processen. Deutsches Archiv. f. klin. Med., lvi.

³ A view held in this country for years by Cabot.

what is usually understood by the term mixed infection, which cannot, with certainty be excluded in any form of tuberculosis.

Kjer-Peterson finds no distinct relationship between the local extent of the changes in the lung and the leukocyte count, both in men and women. The level of the curve seems to be lower the more passive the process. In active cases in women, however, he sometimes has found low values. He finds no constant relation between variations in temperature and the number of leukocytes, and in rapidly progressing cases of the third stage he finds leukocytic curves of either very high or very low level. With a single exception he found that high leukocyte counts were met in cases with very bad prognosis or in which there were other complications (tumor, fetid bronchitis, etc.). Contrary to the usual opinion, therapeutic measures, which would induce decrease, rather than increase, of leukocytes in the capillary blood, would recommend themselves in such cases.

In this work no attempt is made by its author to differentiate the varieties of white cells. In regard to the results of recent investigations in this field we find again a great and confusing divergence in the reports presented. Responsible for this chaotic condition are principally lack of uniformity in classification of the leukocytes and also of the cases, in regard to the stage of the disease. Anything that will promote uniformity in these matters will materially help us to a better understanding of the morbid processes under consideration.

In our counts we have not been able to adopt all the precautions recommended by Kjer-Peterson, his monograph having appeared so recently. Therefore the figures which we obtained and which are given in the tables cannot be compared directly with those obtained by him. They are, however, comparable among themselves and with the results obtained by differential methods of cellular analyses. A more extensive reference to Kjer-Peterson's methods and findings is made here, because in our future studies of the numerical leukocyte relations they shall be based on his technique, and also because it is hoped that other investigations may be made which will allow comparison. All our counts were made four to five hours after the first meal, but no attempt was made to determine the "homogeneity" of the blood. The results of our counts which are tabulated, together with other findings, will be discussed later.

That a differential examination and count of the white cells is necessary in order to determine whether an increase of leukocytes can properly be considered as a "leukocytosis," has occasionally been insisted on. Da Costa,¹ for instance, understands by the term "leukocytosis" an increase of the polynuclear neutrophilic white

¹ Clinical Hematology, London, 1902.

cells. Strauss and Rohnstein¹ observed in chronic pulmonary tuberculosis the following average percentages: multinuclear, 80.8 per cent.; mononuclear, 17.2 per cent.; lymphocytes, 13.1 per cent. They are impressed by the fact that with progressing disease there is a tendency to decrease of the mononuclear percentages. R. Cabot finds little qualitative changes in many cases; sometimes he has noted with a normal leukocyte count an increase of the lymphocytes and large mononuclears. With an increase of the total leukocytes he observed the ordinary marked increase of the polymorphonuclears at the expense of the lymphocytes. He has seen the eosinophiles increased in some cases with cavities, but he does not consider this fact of any particular importance, as have others. Another American observer, Swan, notes in the second and third stages, polynuclear leukocytosis, increase of the eosinophiles, a fact which he considers prognostically favorable.

Holmes² has studied the morphology of the white cells in the blood of tuberculous patients. He believes that tissue destruction goes parallel with disintegration of the white cells and that the degree of regenerative power can be estimated by the intensity of the nuclear stain, the number of intact nuclei, the relatively high percentage of young cells, and the increase of eosinophiles.

Arneth,³ in an exhaustive monograph, has described his method, technique, and results of finer morphological and particularly nuclear studies of neutrophils in infectious diseases, including tuberculosis. In the work above referred to he gives a *resume* of all his investigations in tuberculosis. The neutrophils on account of their predominant numbers (75 to 100 per cent.) among the total of all leukocytes must play, according to him, a most important role in the organism. He divides the neutrophils into five classes: His Class I contains mononuclear neutrophils, Class II, neutrophils with two nuclei or particles of nuclei, Class III three, and so on. He makes, furthermore, subdivisions according to the shape and number of the nuclear subdivisions. A neutrophil of Class I, with an absolutely round nucleus, he designates as myelocyte (M). The other forms in this class with more or less indented nuclei, which he thinks correspond to the polymorphonuclears of other authors, he calls in accordance with the degree of indentation: W. (wenig) for slight, T. (tief) for deep indentations.⁴ In other classes he notes whether there are nuclei in the shape of loops (S-Schlinge) or round nuclear particles (K-runder Kernteil).⁵

¹ Die Blutszusammensetzung bei den verschiedenen Anämien, Hirschwald, Berlin, 1901.

² The Diagnosis of Tuberculosis from the Morphology of the Blood, Medical Record, 1896, and other articles.

³ Die neutrophilen weissen Blut-Körperchen bei Infektions Krankheiten, Gustav Fischer, Jena, 1904.

⁴ In our tables we have adopted the symbols SI and D, according to the English nomenclature.

⁵ In our tables marked as L. and R.

He examines the dried-blood film, stained with Ehrlich's triacid solution, and always determines in each case the total number of leukocytes. By always counting one hundred cells his figures indicate the percentage of the various groups. The various combinations of loops and round nuclei in the neutrophils and the three groups in Class I give a total of twenty subdivisions of his original five classes. This seems at first very complex, but after some experience one learns to classify rapidly the cells according to their respective subdivisions, provided one has a well-stained specimen.

By arranging the numbers found into tables horizontally one next to the other, beginning with Class I at the left end, he receives what he calls a neutrophilic "blood picture." From an average of fifteen single examinations of healthy adults he determines his standard normal neutrophilic blood picture, which we shall give later. He finds this picture altered in pathological conditions, though not parallel with the changes in the total number of leukocytes. He can find a profound alteration of the blood picture with a perfectly normal (5000 to 6000) leukocyte count. His tables give a very clear demonstration of these conditions. Thus he finds it necessary to distinguish different kinds of "cytoses" (abbreviation for leukocytoses); "hyper-," "normo-" and "hypocytoses" indicating increased, normal, and decreased number of leukocytes; and as regards the blood picture, he then distinguishes isocytoses and anisocytoses, *i. e.*, those with normal and those with altered blood picture. Since the numerical findings of the leukocytes do not correspond with the alterations of the blood picture, in order to designate these relations he speaks of anisohypercytoses, isonormocytoses, anisonormocytoses, and anisohypocytoses. The terms here enumerated designate the relations most frequently encountered.

The cells with the more complex nucleus (higher classes) Arneth thinks are the riper and more efficient ones, while the others are the youthful and therefore less efficient types (contrary to Holmes). The pathological alterations of the blood picture are characterized by the disappearance or decrease of the cells from one class and the appearance or increase of cells in another; one can then speak of a shifting of the blood picture to the left or the right. By a great number of examinations of the blood picture in infectious diseases and also in experimental infections and intoxications of rabbits, Arneth has been able to demonstrate a constant and direct relation between the course of the disease and the relations of the picture. The latter are, therefore, an index of the defensive and protective efforts of the body against infections.

Before recording the results of examinations made by ourselves, we shall reproduce some typical blood pictures of his and also some of our own, taken at random from our records. In the tables

below we have, for the sake of simplicity, avoided giving the results of the counts in the lesser subdivisions. Though they have all been made in each case, the sum for each principal class is here given. In a more detailed later report we shall give all the divisions.

Picture 1. Arneth's normal (average of fifteen examinations) neutrophilic blood picture. (Isornormocytosis.)

Actual leukocyte count, 5500	I	II	III	IV	V
	5%	35%	41%	17%	2%

Picture 1 illustrates a normal distribution of various neutrophilic cell types. We see that the types of Classes III and II predominate, with a fair percentage of cells of Class IV. In the picture (2) of a case of acute miliary tuberculosis (patient died nine days later), which is one of successive examinations, we can observe the typical "shifting" of the picture to the left; practically all the cells are crowded into the first two classes. Only the more youthful elements are left to carry on the struggle, and this condition increases with the progress of the case. The total leukocyte count is low.

Picture 2. Miliary tuberculosis, Arneth's Case 1, September 1, 1904. (Anisohypocytosis.)

Actual leukocyte count, 4400	I	II	III	IV	V
	36%	56%	8%		

We find similar conditions in the third picture, which, however, is not taken, as in the last case, from an early series of examinations, but from the last of the series, shortly before the death of the patient. It shows the last phase of continued alteration of the blood picture, with slight hyperleukocytosis.

Picture 3. Subacute (not miliary) tuberculosis, Arneth's Case 5, October 2, 1903. (Anisohypercytosis.)

Actual leukocyte count, 8400	I	II	III	IV	V
	45%	52%	3%		

Picture 4. Chronic pulmonary tuberculosis, stage I A, Case 5(34). (Anisohypercytosis.)

Actual leukocyte count, 7600	I	II	III	IV	V
	14%	37.5%	36%	11%	2%

Picture 4 is derived from one of our few cases which do not show extensive alterations. It is also one of those cases which are very difficult to classify as regards activity or passivity. There is very slight fever, only occasionally, rarely reaching above 100°. A further alteration in the blood picture, observed later, should make the prognosis more unfavorable than a general clinical consideration of the case would allow.

Picture 5. Chronic pulmonary tuberculosis, stage I P, Case 8(37). (Anisornormocytosis.)

Actual leukocyte count, 5800	I	II	III	IV	V
	2.5%	51%	38.5%	8%	

Picture 5 shows a slightly more marked alteration, especially in Class II. Diagnosis is made from the results of physical examination, not verified by the microscope. The patient lost in weight very considerably. By no means a clear case; the low percentage in Class I is remarkable and may perhaps have diagnostic significance, together with the number of leukocytes.

Picture 6. Chronic pulmonary tuberculosis, stage II A, Case 24(52). (Anisohypercytosis.)

	I	II	III	IV	V
Actual leukocyte count, 7600	14%	56.5%	24.5%	4.5%	0.5%

Picture 6 is from a patient with extensive pulmonary lesions and signs pointing to considerable activity of the process. The number of leukocytes is only slightly increased, while the blood picture is markedly shifted to the left. Prognostically, from every view point this is a bad case, though not nearly as extensive in regard to the pulmonary lesions as the two following cases:

Picture 7. Chronic pulmonary tuberculosis, stage III A (8), Case 30(59). (Anisohypercytosis.)

	I	II	III	IV	V
Actual leukocyte count, 8400	56%	38.5%	5.5%	0.5%	0.5%

Picture 8. Chronic pulmonary tuberculosis, stage III P (1), Case 26(54). (Anisohypercytosis.)

	I	II	III	IV	V
Actual leukocyte count, 27,080	29.5%	60%	9%	1.5%	

Pictures 7 and 8 were obtained from far advanced cases with extensive pulmonary lesions. The principal difference in the two blood pictures seems to be in the first two classes and in the leukocyte count. The last case is interesting, for the fact that in spite of very advanced lesions there has been a gain in weight although the blood picture deteriorated.

As regards the "normal neutrophilic blood picture" series of examinations have shown us¹ similar relations to those obtained by Arneth in healthy individuals. The examinations were made at different times of the day in specimens of blood from six individuals, and objectivity of judgment was ensured by independent counts and subsequent comparison of results. A distinct uniformity of results was quite striking, the ratios of distribution of the five principal types of cells being quite constant. We can, therefore, thus far confirm this part of Arneth's results, contrary to Flesch and Schlossberger,² who on examination of twenty-six normal individuals, mostly children, found a very different numerical distribution of the cells in the five classes. They, however, recognize also a fairly uniform "normal" picture.

Further serial examinations of neutrophilic pictures of healthy

¹ Reported at the meeting of the Chicago Pathological Society, April, 1906, by Drs. Hall and H. Klebs.

² Die Veränderungen des neutrophilen Blutbildes, Jahrbuch f. Kinderheilkunde, 1905.

individuals of both sexes, at various age periods, and under different external influences, seem most desirable and we have planned such investigation on a larger scale. The technique of the method is quite simple; particular attention is necessary to ensure thin blood smears. Undue pressure in the spreading of the blood on the cover-glass can lead directly or indirectly to a distortion of the cells and so artificially modify the picture. That the spreading, drying, fixing, and staining of the blood has a direct influence on the shape of the nuclei is forcibly suggested by the photographs recently obtained, by means of the ultra-violet light (Ernst, Grawitz), of polymorphonuclear leukocytes not previously prepared. In these the nuclei do not seem to have the complex conformation seen in the stained specimens. Further improvement in the technique of ultra-violet photography, however, is necessary before pictures obtained by it can be compared with the stained specimens. The stain used by Arneth is the triacid solution of Ehrlich, not a good nuclear stain, a fact which he thinks is rather of advantage, because it avoids too great detail in the nucleus. In our examinations various stains have been tried, and we found that for proper differentiation of nuclear forms the triacid solution gave very unsatisfactory results. For this reason, Wright's stain has been employed in most instances, with better result. At least one hundred cells have been counted at each examination and in different specimens. The accurate and minute classification of the cells constitutes the principal difficulty of the method. The proper distribution of the cells, however, into the principal classes is not so difficult, and for practical clinical purposes this probably suffices.

The uniformity which the normal blood pictures maintain with varying total leukocyte figures impressed us particularly.

The blood pictures shown above as examples on the whole confirm Arneth's observations. All of them except 4 and 5 show marked alterations. A material so uniformly bad as ours does not permit far reaching conclusions as regards prognosis. An interpretation of the finer changes in our blood pictures is quite difficult and ought to be made with caution, and it will need many further examinations and technical improvements to make the method more serviceable. In the following table we have arranged the cases according to the alteration of the neutrophilic picture, which they presented, beginning with those in which the alteration was slightest. This arrangement is not absolutely correct, because it is based upon the sum of cells found in the first two classes only. A variation between these two classes, as frequently observed and perhaps of considerable importance, therefore, is not taken into account in this arrangement. It seemed to us, however, of advantage to range the cases by some approximative method for purposes of a general survey.

Serial No.	Case No.	I + II	Leuko-cyte counts.	Stage.	Sex and age.	Remarks.
1	28 (56)	41	17,000	II A	M. 42	Operated for appendicitis, retroversion, pleurisy, lymphocytes above normal.
2	5 (34)	51	7,300	I A	F. 21	
3	7 (85)	52	4,350	III A ₂	M. 77	Emphysema, tabes dorsalis, died day after.
4	8 (37)	54	5,800	I P	F. 27	Asthma, bronchitis, no tubercles, increase of eosinophiles 7 per cent.
5	29 (58)	55	9,800	III P ₁	M. 51	Thrombus of right brachial.
6	27 (55)	59	7,900	III A ₂	M. 35	Unconscious, died in night.
7	22 (50)	64	9,200	III A ₂	M. 40	Unconscious, dying.
8	10 (38)	66	5,500	I P	M. 29	Scoliosis, gain in weight, well nourished, drinker.
9	25 (53)	67	(a) 12,500	III A ₁ b	M. 27	Large cavity, abundant sputum.
			12,300			
10	24 (52)	71	7,600	II A	F. 29	Epileptic.
11	20 (48)	73	14,200	III A ₁ b	M. 28	Marked pleurisy.
12	16 (44)	74	15,570	III A ₂	M. 36	Cavity, abundant sputum.
13	18 (46)	75	7,100	III A ₁ b	M. 55	Cavity.
14	31 (60)	75	6,230	III P ₁	M. 48	Very chronic type, twenty years, able to work.
15	4 (33)	75	9,000	III A ₂	M. 30	Acute nephritis, syphilis, small loss in weight, drinker.
16	13 (41)	76	10,400	III A ₁ b	M. 27	Abundant sputum, losing in weight.
17	15 (43)	76	9,200	III A ₂	M. 42	Mitral regurgitation, large cavity, abundant sputum, drinker.
18	11 (39)	79	8,640	III A ₂	M. 48	Suspected cavity, hemoptysis, lymphocytosis.
			13,500			
19	19 (47)	80	9,400	II P	M. 26	
20	23 (51)	81	7,560		M. 35	
21	32 (61)	82	16,400	III A ₂	M. 21	Large cavity, hemoptysis, lymphocytes normal.
22	12 (40)	83	5,000	III A ₂	M. 40	Cavity, profuse hemoptysis, syphilis, lymphocytosis (losing).
23	3 (32)	83	17,321	III A ₂	M. 32	Large cavity, large quantity sputum, numerous tubercles, drunkard, rapidly losing in weight.
			12,400			
24	1 (30)	83	19,000	III A ₂	M. 42	Cavity, pneumothorax, hemoptysis, abundant sputum.
			18,400			
25	6 (35)	87	9,700	III A ₂	F. 18	Cavity, moderate quantity sputum, lymphocytosis.
			10,555			
26	9 (38)	87	13,500	III A ₂	M. 33	Rapid decline.
27	17 (45)	88	17,200	III A ₂	F. 47	Generally firm, oedema, died in evening.
28	14 (42)	90	6,770	III A ₂	M. 38	Dying.
			7,600			
29	26 (54)	90	3,300	III P ₁	M. 21	Scoliosis, tuberculous coxalgia, cavity, gain in weight.
30	21 (49)	91	32,800	III A ₂	M. 26	Lymphocytes markedly subnormal.
31	30 (59)	94	27,080	III A ₂	M. 50	Large cavity, great emaciation, delirious.
32	2 (31)	95	8,400	II A	M. 16	Tuberculous peritonitis, fecal fistula, splenic tumor.
			8,950			
			11,120			
			12,300			

If we compare the figures in the two columns of the neutrophilic pictures and the total leukocyte count we find with increasingly damaged blood pictures every degree of normocytoses or hypercytoses. On the whole, however, there appear with increasing alterations of the blood pictures also the higher numbers of leukocytes. The exceptions are quite evident, but an interpretation of the discrepancies is very difficult. Several of our figures were obtained from single observations only, and since variations occur, we probably should have had to modify them after frequent repetitions of the examinations. In studying the table this defect must be considered.

Examples of cases with a damaged blood picture but with normal or nearly normal leukocyte numbers are found in cases (serial Nos.) 13, 14, 15, 17, 18, 19, 21, 27, 28, 31. They are all prognostically very unfavorable cases. Arneth thinks that the particularly unfavorable aspect of these cases is due to the disproportion existing between the production of young and the destruction of older cells. The young cells are just sufficient in number to counterbalance the loss of older cells without being able to fill the deficit. If hypercytotic figures are reached the deficit can be supplied and the prognosis becomes better. That this does not always bring about an improvement of the picture and the condition of the patient the greater number of our cases demonstrates.¹

The more or less profound alteration of the neutrophilic picture which we have observed in all the severe cases of tuberculosis, with very few exceptions, seems in general to confirm Arneth's statements. Prognostically, we could not draw valuable conclusions from the condition of blood pictures, which in itself is of no particular significance, considering the preponderant majority of far advanced cases. Examination of patients in the first and second stages, and also of patients treated with tuberculin which we have begun, will throw further light on the question. The method would certainly have the advantage of simplicity over others, particularly that of determination of the opsonic index, and for that reason alone, further investigations along these lines seem desirable. This preliminary report is intended to induce such.

FURTHER NOTES ON THE SERUM DIAGNOSIS OF TUBERCULOSIS.²

BY HUGH M. KINGHORN, M.D.,

AND

DAVID C. TWICHELL, M.D.,

OF SARANAC LAKE, NEW YORK.

(From the Saranac Laboratory, Dr. E. L. Trudeau, Director.)

At the meeting of the National Association for the Study and Prevention of Tuberculosis held in Washington in May, 1905, one of us reported the results obtained with the serum diagnosis of tuberculosis. The method used was that of Arloing and Courmont, and their A homogeneous culture was employed.

¹ An interesting feature in our material is the fact that there are several cases with both tuberculous and syphilitic lesions. In how far this fact can affect the blood picture cannot be surmised from the small number observed.

² Read at the meeting of the National Association for the Study and Prevention of Tuberculosis, Washington, D. C., May 17 and 18, 1906.